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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,169	12/06/2000	Daniel R. Henderson	CELL-004CON	6741

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EXAMINER
WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
1635	14

DATE MAILED: 08/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/732,169	Applicant(s) HENDERSON ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8 and 55-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8 and 55-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 October 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Final Rejection

Claims 1, 3-8, and 55-80 are pending examination.

Applicants' traversal, addition of claims 77-80, cancellation of claim 2, amendment to claims 1, 3-8, and 55-76 in paper no. 13 are acknowledged and considered.

Priority

It is noted that this application appears to claim subject matter disclosed in prior application 09/033,555 filed on 3/2/98. The current status of all non-provisional parent applications referenced should be included. 09/033,555 appears to be abandoned. Appropriate correction is required.

Drawings

NOTE: In the next response, please submit a response to the PTO 498 because a PTO 498 was filed with the non-final rejection paper no. 9 and the applicants have not submitted proposed corrections to the drawings. If the reply to the Final Rejection does not have a response to the 498, the response will be considered non-responsive. See 37 CFR 1.85(a).

Double Patenting

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time-wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8, 59, 61, and 67 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable as that of claims 1-8, 28-31, 33-34, 42, and 44-45 of co-pending Application No. 09/151,376. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Applicants submit that when a provisional rejection of this type is made, it is proper to issue one of the applications and allow a terminal disclaimer to be filed in the other, and agree to provide a suitable terminal disclaimer at such time as a patent is issued. See page 6.

Claims 1-6, 8, 59, 61, and 67 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable as that of claims 1, 3-6, 8-9, and 12 of US Patent No. 5,698,443. For example, claim 5, of patent '443 is drawn to an adenovirus vector comprising at least one of the genes E1A, E1B, or E4 under transcription control of a prostate cell specific response element.

Applicants agree to provide a terminal disclaimer for the present claims over US Patent No. 5,698,443 as appropriate, upon indication of allowable subject matter. See page 6.

Claims 1-5, 7-8, 59, 61-62, 64-69, and 71-76 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable as that of claims 1-5, 12-14, 21-23, and 27-32 of U.S. Patent No. 5,871,726. The claims 1-4, 12-13, 21-23, and 27-32 of patent '726 are drawn to an adenovirus vector comprising an adenovirus gene essential for propagation under transcriptional control of a prostate specific response element, said prostate cell specific response element comprising an enhancer specific for prostate specific for prostate

specific antigen and a promoter or the adenovirus described above further comprising a transgene, wherein the transgene under transcriptional control of a prostate specific response element (column 41 and 42, claims 1-3). In addition, the claims of the patent are drawn to an in vitro cell comprising either vector described above (column 43, claims 12-14). Furthermore, the claims of the patent are drawn to a method of propagating either adenovirus vector described above into a tumor cell (column 43, claims 21-22) or a method of suppressing tumor growth comprising introducing the either adenovirus vector described above into a tumor cell (column 44, claims 27-32). The claims 21-23, and 27-32 of patent '726 are drawn to a method of propagating either adenovirus vector described above into a tumor cell (column 43, claims 21-22) or a method of suppressing tumor growth comprising introducing the either adenovirus vector described above into a tumor cell (column 44, claims 27-32).

Although the conflicting claims in the instant application and patent '726, are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patent uses the adenovirus vector encompassed in the instant application. The difference between the claims of the instant application and patent '726 is that the application encompasses the adenovirus vector that is used in the methods of patent '726. Therefore, the claims of the instant application and patent '726 are obvious variants of one another.

Applicants agree to provide a terminal disclaimer for the present claims over US Patent No. 5,871,726 as appropriate, upon indication of allowable subject matter. See page 6.

Claims 1-5, 7, 59, 61, 64, 67-68, and 71-76 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 14-16, 18, 20, 23-27, 30, 32, and 37-38 of U.S. Patent No. 6, 197,293. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims 1-6, 12, 14-16, 18, 20, 23-27, 30, 32, and 37-38 of patent '293 are drawn to a replication competent adenovirus vector comprising an adenovirus gene under transcriptional control of a probasin transcriptional regulatory element (PB-TRE), wherein the adenoviral gene is essential for replication (claims 1-6 and 23-26) and a host cell comprising the adenovirus vector (claim 16). In addition, the claims of the patent are drawn to the vector described above further comprising a heterologous gene under transcriptional control of PB-TRE (claims 15, 37-38). The claims 14, 18, 30, and 32 of patent '293 are drawn to a method for propagating the vector in cells (claims 18 and 30). The claims of the patent are also drawn to a method of suppressing tumor growth by contacting tumor cells the vector (claims 20 and 32).

Although the conflicting claims in the instant application and patent '293, are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patents use the adenovirus vector encompassed in the instant application. The difference between the claims of the instant application and patent '293 is that the application encompasses the adenovirus vector that is used in the methods of patent '293. Therefore, the claims of the instant application and patent '293 are obvious variants of one another.

Applicants agree to provide a terminal disclaimer for the present claims over US Patent No. 6,197,293 as appropriate, upon indication of allowable subject matter. See page 6.

Claims 1-5, 56-59, 61-66, and 68-73 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-6, 11, and 37 of US Patent No. 6,254,862. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims 1, 3-6, 11, and 37 of patent '862 are drawn to a replication competent adenovirus vector comprising E1A and E1B wherein E1A and E1B are both under transcriptional control of separate alpha fetoprotein transcription elements (AFP-TRE), wherein at least one AFT TRE comprises either an enhancer or a promoter from an AFP gene (claims 1, 3-6) and a host cell comprising the vector described above (claim 11). In addition, the claims of the patent are drawn to a method of suppressing tumor growth in an individual be contacting a tumor cell with the adenovirus vector (claim 37).

Although the conflicting claims in the instant application and patent '862 are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patents use the adenovirus vector encompassed in the instant application. The difference between the claims of the instant application and patent '862 is that the adenovirus is patent '862 is a replication competent adenovirus vector comprising two adenoviral genes, which are both under control of an AFP-TRE. Therefore, the claims of the instant application and patent '862 are obvious variants of one another.

Applicants agree to provide a terminal disclaimer for the present claims over US Patent No. 6,254,862 as appropriate, upon indication of allowable subject matter. See page 6.

Claim Rejections - 35 USC § 112

The rejection under 112, first paragraph is moot in view of the amendment to the claims. See page 7.

The rejection under 112, second paragraph is moot in view of the amendment to the claims and cancellation of claim 2. See pages 6-7.

Claim Rejections - 35 USC § 102

The rejection under 35 U.S.C. 102(b) for claims 1-3, 5-6 and 55 as being anticipated by Friedman et al. is moot in view of the amendment to the claims. See pages 7-8.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-6, 8, and 55-77 are rejected under 35 U.S.C. 102(e) as being anticipated by Gregory et al. (US20001/0053768, filing date 5/3/95). Gregory teaches a method of treating mammalian cancer cells, comprising administering a replication competent adenoviral vector comprising a therapeutic gene and a disease specific gene regulatory region operationally linked to at least one replication gene wherein the cancer cells activate the tumor specific gene regulatory region causing the adenoviral to replicate (page 7, claim 1). Furthermore, Gregory teaches using the alpha-fetoprotein promoter/enhancer, the carcinoembryonic antigen

promoter/enhancer, the prostate specific antigen promoter/enhancer, or the tyrosinase promoter/enhancer (page 7, claims 2, 4, 7, 9, respectively). Gregory further teaches that the replication gene used for making the vector in the method described above is a viral E1 genes, E2 gene, or E4 gene (page 7, claims 16-18).

Applicants traverse the rejection under 102(e) for the following reasons: Gregory et al. is directed to expression of a therapeutic gene from the replication competent adenoviral vectors and specifically not present in the wild-type virus in the targeted tissue; In contrast, Applicants invention is directed at replication competent adenovirus which utilize cell type specific TRE operably linked to native adenoviral genes; In contrast, to the teaching of Gregory, the present invention relies on selective cytolysis of target cells. See page 7.

Applicants' traversal is acknowledged and is not found persuasive for the following reason(s): Gregory teaches production of a replication competent adenoviral vector comprising a TRE operatively linked to an adenoviral early gene (e.g. E1a) and a therapeutic gene inserted in place of the adenoviral E3 gene (See Figure 1, pages 2 [0016], and Example 1, page 5). Gregory further teaches that this modification restrict virus replication to those tumors which utilize the tumor specific promoter/enhancer inserted in place of the E1a promoter (page 2). The scope of the claimed invention embraces a replication competent adenovirus vector **comprising** an adenovirus gene essential for replication under transcriptional control of a cell type-specific transcriptional response element (TRE) and further including a transgene (See pages 40-41 of the as-filed specification). Furthermore, the adenoviral vector taught by Gregory is the same structure as applicants adenoviral vector and thus would possess cytolytic property as claimed by applicants.

Therefore, the rejection under 102(e) remains.

Claim Rejections - 35 USC § 103

The rejection under 103(a) as unpatentable over McCormick, taken with Glazenburg, Berkner, Roth is moot in view of the applicants' traversal.

The rejection under 103(a) as unpatentable over McCormick, taken with Glazenburg, Berkner, Roth in further view of Bohinski, Abe, Grooteclaes, Richards, Vile, Riegman and Watanabe is moot in view of the applicants' traversal.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, and 55 remain and 77-80 are rejected under 35 U.S.C. 103(a) as being unpatentable by Gregory et al. (US20001/0053768, filing date 5/3/95) taken with Bohinski et al. (Mol Cell Biol, Vol. 14, 1993, abstract), Abe *et al.* (PNAS, Vol. 90, 1993, abstract), Grooteclaes et al., (Cancer Res., Vol. 54, abstract, 1994). Gregory teaches a method of treating mammalian cancer cells, comprising administering a replication competent adenoviral vector comprising a therapeutic gene and a disease specific gene regulatory region operationally linked to at least one replication gene wherein the cancer cells activate the tumor specific gene regulatory region causing the adenoviral to replicate (page 7, claim 1). Furthermore, Gregory teaches using the alpha-fetoprotein promoter/enhancer, the carcinoembryonic antigen (CEA) promoter/enhancer, the prostate specific antigen promoter/enhancer, or the tyrosinase promoter/enhancer (page 7, claims 2, 4, 7, 9, respectively). Gregory further teaches that the replication gene used for making the vector in the method described above is a viral E1 genes, E2 gene, or E4 gene (page 7, claims 16-18). Gregory does not an adenovirus vector comprising an adenovirus gene under transcriptional control of a cell type specific transcriptional response element (TRE), wherein the TRE is selected from the group consisting of a DF3-TRE, a surfactant TRE, and an ErbB2-TRE.

Regarding claims drawn to specific TREs, Abe, Grooteclaes, and Bohinski teach that tissue-specific promoters including DF3, surfactant, and ErbB2 are known in the art at the time the invention was made.

It would have been obvious for one of ordinary skill in the art to have modified the adenovirus vector taught by combining Gregory with taken with Bohinski, Abe, Grooteclaes, to produce an adenovirus vector comprising an adenovirus gene under transcriptional control of a cell type specific transcriptional response element (TRE), wherein the TRE is selected from the group consisting of a DF3-TRE, a surfactant TRE, and an ErbB2-TRE. It would also have been obvious for one of ordinary skill in the art to have constructed and employed the tissue-specific-replication competent adenoviral vectors by using a known tissue-specific promoter operably linked to a viral gene necessary for adenoviral replication for expressing a cytotoxic gene in a tumor cell-specific fashion in order to target and deliver the cytotoxic gene product to tumor cells. One of ordinary skill in the art would have a reasonable expectation of success in constructing and employing the tissue-specific-replication competent adenoviral vectors, particularly since Abe, Grooteclaes, and Bohinski all teach that tissue-specific promoters including DF3, surfactant, and ErbB2 are known in the art at the time the invention was made and employed for delivery of gene products to targeted cells.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicants traverse the rejection under 103(a) for the following reasons: As discussed above, Gregory fails to teach a cytolytic replication competent adenovirus, and is directed to adenovirus as a vector to deliver therapeutic foreign genes to a targeted cell; The secondary reference fail to remedy the deficiencies of Gregory. See page 8.

Applicants' traversal is acknowledged and is not found persuasive for the following reason(s): Gregory teaches production of a replication competent adenoviral vector comprising a

TRE operatively linked to an adenoviral early gene (e.g. E1a) and a therapeutic gene inserted in place of the adenoviral E3 gene (See Figure 1, pages 2 [0016], and Example 1, page 5). Gregory further teaches that this modification restrict virus replication to those tumors which utilize the tumor specific promoter/enhancer inserted in place of the E1a promoter (page 2). The scope of the claimed invention embraces a replication competent adenovirus vector **comprising** an adenovirus gene essential for replication under transcriptional control of a cell type-specific transcriptional response element (TRE) and further including a transgene (See pages 40-41 of the as-filed specification). Furthermore, the adenoviral vector taught by Gregory is the same structure as applicants adenoviral vector and thus would possess cytolytic property as claimed by applicants. More specifically, Gregory teaches production of a replication competent adenoviral vector comprising a TRE operatively linked to an adenoviral early gene and a therapeutic gene inserted in place of the adenoviral E3 gene (See Figure 1, pages 2 [0016], and Example 1, page 5). Gregory further teaches that this modification restrict virus replication to those tumors which utilize the tumor specific promoter/enhancer inserted in place of the E1a promoter (page 2).

Furthermore, regarding claims drawn to specific TREs, Abe, Grooteclaes, and Bohinski teach that tissue-specific promoters including DF3, surfactant, and ErbB2 are known in the art at the time the invention was made. Therefore, it would also have been obvious for one of ordinary skill in the art to have constructed and employed the tissue-specific-replication competent adenoviral vectors by using a known tissue-specific promoter operably linked to an adenoviral gene necessary for adenoviral replication for expressing a cytotoxic gene in a tumor cell-specific fashion in order to target and deliver the cytotoxic gene product to tumor cells. One of ordinary skill in the art would have a reasonable expectation of success in constructing and employing the

tissue-specific-replication competent adenoviral vectors, particularly since Abe, Grooteclaes, and Bohinski all teach that tissue-specific promoters including DF3, surfactant, and ErbB2 are known in the art at the time the invention was made and employed for delivery of gene products to targeted cells.

Therefore, the rejection under 103(a) remains.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kay Pinkney whose telephone number is (703) 305-3553.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775.

The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, primary examiner, Dave Nguyen can be reached at (703) 305-2024.

If attempts to reach the primary examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DAVE T. NGUYEN
PRIMARY EXAMINER

Brian Whiteman
Patent Examiner, Group 1635
8/23/02